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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Walker JG, Kuchuloria T, Sergeenko D, et al. Interim effect evaluation of the hepatitis C elimination programme in Georgia: a modelling study. *Lancet Glob Health* 2019; published online Dec 18. http://dx.doi.org/10.1016/S2214-109X(19)30483-8.

Table of Contents

Supplementary Methods

Model Structure

Summary

The framework of the model used is based on a traditional SI (susceptible-infected) model, with an additional compartment T representing the population undergoing treatment (Figure 1A). Each of these compartments is stratified in 4 dimensions: (1) 3 PWID strata (non-, current, and ex-PWID; Figure 1C); (2) 5 liver disease state strata (none/mild liver disease or F0-F1, moderate liver disease or F2-F3, compensated cirrhosis or F4, decompensated cirrhosis, and hepatocellular carcinoma; Figure 1B); (3) 9 age group strata (<15, 15-17, 18-24, 25-29, 30-34, 35-39, 40-44, 45-50, and 50+; Figure 1C); and (4) 2 gender strata (male and female). The full model therefore contains 810 equations representing each possible combination of compartments. The model was initialized in 1900 with a population size of 4 million, all susceptible, non-PWID, and with no liver disease, distributed equally across gender and age compartments.

The model progresses as follows. Each year, B individuals are born into the susceptible category in the youngest age group, equally divided between males and females. These individuals age at age-group specific rates α and die at age and gender-specific rates μ. Susceptible individuals become infected at a force of infection λ according to the ratio of infected to susceptible population sizes and PWID status, with a rate of transmission β for the whole population, and an additional rate of transmission θ for current PWID, with the force of infection also accounting for the coverage of harm reduction interventions. The infected population starts treatment at rate σ and completes treatment at rate ω, either entering the susceptible or infected populations according to the cure rate π. Non-PWID transition to PWID at gender-and age-specific rates ψ and PWID cessate from injecting at age-specific rates ϕ and have an additional drug-related death mortality ratio ν. If infected, the population in the none/mild liver disease state progress through moderate liver disease to compensated cirrhosis at rates γ, and do not progress through these states if cured. Progression from compensated cirrhosis to decompensated cirrhosis or hepatocellular carcinoma (HCC) occurs at rates χ, with reduced progression rates for those that are no longer infected due to successful treatment. HCV-related death occurs from decompensated cirrhosis and hepatocellular carcinoma at rates ζ.

Equations

$S_{k,n}^{i,j}$, $I_{k,n}^{i,j}$, and $T_{k,n}^{i,j}$ are the number of susceptible, chronically infected, and on treatment individuals in the model, respectively. Superscript $i = 1,2,3,4,5$ represents disease progression states (1) none/mild liver disease, (2) moderate liver disease, (3) compensated cirrhosis, (4) decompensated cirrhosis, and (5) hepatocellular carcinoma. Superscript $j = 1,2 \ldots 9$ represents age groups <15, 15-17, 18-24, 25-29, 30-34, 35-39, 40-44, 45-50, and 50+, respectively. Subscript $k = 1,2,3$ represents non-PWID, PWID, and ex-PWID, respectively. Subscript $n = 1,2$ represents male and female gender, respectively. Subscript $m = S, I, T$ for parameters which vary by infection state; some parameters are also functions of time (t).

Inflows and outflows from each compartment are due to birth ($B_n^{j=1}$) and death (μ_n^j, ν_k, ζ^i), disease progression (γ_m^i, χ_m^i), aging (α^j), recruitment ($\psi_{k=1,n}^j(t)$) and cessation ($\phi_{k=2}^j$) of injecting drug use (IDU), treatment ($\sigma_k^i(t)$), and cure ($\omega, \pi(t)$). The treatment parameter $\sigma_k^i(t)$ was calculated as the ratio of number of treatments implemented per infected individuals in the model at each time

point (see Treatment section below). HCV transmission occurs through the force of infection ($\lambda_k^j(t)$), as described below.

The basic structure of the model is therefore:

$$\frac{dS_{k,n}^{i,j}(t)}{dt} = B_n^{j=1} + \left[-\left(\mu_{n,k}^j + \zeta^i\right) + \gamma_S^i + \chi_S^i + \alpha^j + \psi_{k=1,n}^j(t) + \phi_{k=2}^j - \lambda_k^j(t)\right]S_{k,n}^{i,j}(t) + \omega\pi(t)T_{k,n}^{i,j}(t)$$

$$\frac{dI_{k,n}^{i,j}(t)}{dt} = \left[-\left(\mu_{n,k}^j + \zeta^i\right) + \gamma_I^i + \chi_I^i + \alpha^j + \psi_{k=1,n}^j(t) + \phi_{k=2}^j - \sigma_k^i(t)\right]I_{k,n}^{i,j} + \lambda_k^j(t)\,S_{k,n}^{i,j}(t) + \omega(1-\pi(t))T_{k,n}^{i,j}(t)$$

$$\frac{dT_{k,n}^{i,j}(t)}{dt} = \left[-\left(\mu_{n,k}^j + \zeta^i\right) + \gamma_T^i + \chi_T^i + \alpha^j + \psi_{k=1,n}^j(t) + \phi_{k=2}^j - \omega\right]T_{k,n}^{i,j}(t) + \sigma_k^i(t)I_{k,n}^{i,j}(t)$$

The force of infection $\lambda_k^j(t)$ is determined by the degree of assortative mixing (M) amongst PWID by age group (<30, $j \leq 4$ versus ≥30, $j \geq 5$), the impact and coverage of harm reduction measures (NSP and OST, $\varphi(t)$), general population HCV transmission parameter β, reduction in general population transmission parameter $\epsilon(t)$, and PWID HCV transmission parameter θ, where $N(t) = S(t) + I(t) + T(t)$:

For all non-PWID:

$$\lambda_{k=1,3}(t) = \beta\epsilon(t)\frac{I(t)}{N(t)}$$

For young PWID:

$$\lambda_{k=2}^{j\leq 4}(t) = \beta\epsilon(t)\frac{I(t)}{N(t)} + \theta\varphi(t)\left[(1-M)\frac{I_{k=2}(t)}{N_{k=2}(t)} + M\frac{I_{k=2}^{j\leq 4}(t)}{N_{k=2}^{j\leq 4}(t)}\right]$$

For old PWID:

$$\lambda_{k=2}^{j\geq 5}(t) = \beta\epsilon(t)\frac{I(t)}{N(t)} + \theta\varphi(t)\left[(1-M)\frac{I_{k=2}(t)}{N_{k=2}(t)} + M\frac{I_{k=2}^{j\geq 5}(t)}{N_{k=2}^{j\geq 5}(t)}\right]$$

Where in the base case (high intervention impact; see Impact of Harm Reduction section below for more details) the impact of OST and NSP are determined by OST coverage ($\varrho_o(t)$), OST effectiveness (ρ_o), and NSP-associated impact $\rho_n(t)$:

$$\varphi(t) = (1 - \varrho_o(t) + \varrho_o(t)\rho_o)\rho_n(t)$$

In the alternative scenario (low intervention impact), NSP is determined by coverage ($\varrho_n(t)$) and effectiveness (ρ_n), such that:

$$\varphi(t) = \left(1 - \varrho_o(t) - \varrho_n(t) + \left(\varrho_o(t)\varrho_n(t)\right)\right) + \varrho_o(t)\rho_o\left(1-\varrho_n(t)\right) + \varrho_n(t)\rho_n\left(1-\varrho_o(t)\right) + \varrho_o(t)\varrho_n(t)\rho_o\rho_n$$

Parameter Definitions

Parameters used in the model are either fitted (see Model Calibration section and Supplementary Tables 2-5) or input as single values, as described below. All rates are annual.

Demographics

The annual number of births $B_n^{j=1}$ is assumed to be equal for males and females and to remain constant over time; this parameter is fitted to achieve the target population size with a prior range from 51,000 to 62,000. Aging (α^j) rate is defined as the inverse of the duration spent in each category (Supplementary Table 1). The base death rate $\mu_{n,k}^j$ varies by age and sex (Supplementary Table 1), these values were adapted from the WHO Global Health Observatory data repository life tables for the country of Georgia for 2010-2015 (http://apps.who.int/gho/data/view.main.60610?lang=en). For PWID (k=2), the base death rates are scaled by ν, with $\mu_{nk=2}^j = \nu\mu_n^j$ for active PWID, to represent the additional risk of death for active PWID (Supplementary Table 2).

Injecting drug use

Recent estimates from 2007-2014 suggest a stable PWID population in Georgia of about 50,000[1], however, data from 1998-2015 suggest an aging PWID population, likely due to reduced initiation of injecting (Supplementary Figure 1). To account for the changing dynamics of IDU in Georgia, we assumed a transient peak in the initiation of IDU, allowing considerable uncertainty in when this occurred and its magnitude. Recruitment to injecting drug use $\psi_n^j(t)$ is assumed to start in 1960, which is the first year of reported injecting in all available biological and behavioural surveillance (BBS) surveys, scale up in year τ_2 by δ_1, and decline in year $\tau_2 + \Delta$ by δ_2 (Supplementary Table 2). Therefore for non-PWIDs (k=1), the rate of recruitment to IDU is:

$$\psi_n^j(t) = \begin{cases} 0, & t < 1960 \\ \psi_0\ , & 1960 \le t \le \tau_2 \\ \psi_0\ \delta_1, & \tau_2 < t \le \tau_2 + \Delta \\ \psi_0\ \delta_1/\delta_2, & \tau_2 + \Delta < t \end{cases}$$

Where for males (n = 1), $\psi_0 = \begin{pmatrix} 0.02\psi \\ 0.24\psi \\ 0.62\psi \\ 0.09\psi \\ 0.02\psi \\ 0.01\psi \\ 0 \\ 0 \\ 0 \end{pmatrix}$, and for females (n=2), $\psi_0 = f_\psi \begin{pmatrix} 0.02\psi \\ 0.24\psi \\ 0.62\psi \\ 0.09\psi \\ 0.02\psi \\ 0.01\psi \\ 0 \\ 0 \\ 0 \end{pmatrix}$.

Proportions of PWID recruited into each age group were calculated from the distribution of ages in which PWID reported starting injecting within the BBS. We assume that once an individual has cessated injecting they do not restart.

The rate of cessation from injecting ($\phi_{k=2}^j$) is fit individually to three age groups of PWID, with separate rates for age groups <29 years, 30-49 years, and 50+ years. The model also allowed for the possibility of assortative 'like-with-like' mixing when young (<30 years) and older (>30 years) PWID form transmission contacts, varying between random mixing across these age groups to

preferential mixing only between PWID of the same age group, according to the fitted parameter M (Supplementary Table 2).

HCV transmission

We fit separate transmission parameters for transmission of HCV in the general population (β) and PWID (θ), which represent the annual effective contact rates of transmission within the force of infection equation above (Supplementary Table 3). The rates of transmission are fit to prevalence of chronic infection so spontaneous clearance of infection is not explicitly modelled. Hepatitis C is introduced to the model in 1960, when IDU is assumed to have started, with any cases of hepatitis C prior to this time assumed to no longer be alive. To generate a rapid increase in infection amongst PWID, hepatitis C is seeded in the model with a 10% annual rate of infection for susceptible PWID < 30 years old in the first five years after 1960.

HCV transmission in the general population is assumed to decline over time, with a reduction at time point τ_3, by the ratio ϵ, due to increasing awareness of blood-borne virus transmission routes leading to reductions in medical risks (Supplementary Table 3). We assume this coincides with restructuring of the health system and the introduction of new regulations including donor blood screening from 1997[2,3]. HCV transmission due to IDU changes over time through harm reduction measures as described in the next section.

Impact of Harm Reduction

Harm reduction measures were introduced in Georgia in the early 2000s, including voluntary counselling and testing, needle and syringe provision (NSP), and opioid substitution therapy (OST); NSP was introduced in 2001 and OST in 2005 with both gradually increasing over time[4,5]. The impact of NSP and OST at reducing HCV transmission have been estimated in a recent global Cochrane review[6]. We use the global effectiveness estimate from this review for the OST effectiveness parameter ρ_o, with two alternative methods for estimating the effectiveness of NSP (Supplementary Table 4).

Initially, we fit a **low intervention effect** model scenario which uses values for the impact of NSP from the Cochrane review[6], and reported NSP coverage[5], which is presented in the sensitivity analysis. Model calibration scenarios had to agree with current epidemic patterns amongst PWID and the general population. However, the low intervention effect model did not capture the observed decline in hepatitis C prevalence in young PWID, instead fitting a relatively low hepatitis C incidence in PWID through the whole time period. Therefore, a new structure for the impact of NSP, the **high intervention effect** model, was developed and fit to the observed halving of hepatitis C prevalence in young PWID between 2002 and 2015. The **high intervention effect** model is the primary scenario presented in the main text. This calibration freely varies the efficacy of NSP interventions in the model to ensure it closely agreed with the observed large reduction in the prevalence of hepatitis C amongst young PWID over the last 20 years (decreased from 62% in 1997 to 29% in 2015, Supplementary Figure 2). To match this, we fit an initial reduction in PWID transmission in 2002, when a large project on prevention of HIV/AIDS was initiated[7]. We assume the initial change in PWID HCV transmission (ρ_{2002}) varies linearly over 10 years towards an independently sampled value for reduction in PWID transmission which is constant from 2012 onwards (ρ_{2012}). Finally, we fit the model to the same summary statistics without allowing a peak in PWID recruitment, in order to evaluate the importance of this peak in producing model fits.

When looking at hepatitis C sero-prevalence data across cities with repeated BBS PWID surveys, the overall prevalence of hepatitis C amongst PWID in Batumi and Tbilisi increased by 16% (relative increase) for 2006-2015, and by 29% in Kutaisi for 2007-2015; the more conservative increase from the larger populations in Batumi and Tbilisi was used for model fitting.

Liver disease progression

Progression through liver disease states occurs after HCV infection, and is modelled according to Metavir stages (F0-F4)[8]. The population in the none/mild liver disease state (F0-F1) transitions to moderate liver disease (F2-F3) at annual transition probability γ^1, and then to compensated cirrhosis (F4) at rate γ^2. After hepatitis C is cured through treatment, it is assumed that susceptible individuals do not continue to progress through liver disease from the mild or moderate liver disease states. After reaching compensated cirrhosis, progression to decompensated cirrhosis occurs at annual transition probability χ^3, with progression reduced by ratio χ^{HR1} for HCV-susceptible individuals. Similarly, those with compensated or decompensated cirrhosis progress to HCC according to parameter χ^4, which is scaled by χ^{HR2} for HCV-susceptible individuals. HCV-related death occurs only from states of decompensated cirrhosis (ζ^4) and hepatocellular carcinoma (ζ^5). The values were estimated from published studies[9–11], with the uniform prior range representing the 95% confidence intervals of reported transition probabilities (Supplementary Table 5). The parameters were then fitted in the model fitting process, however, the posteriors were expected to remain similar to the priors as there were no summary statistics likely to restrain them.

Treatment

Prior to the elimination program, between 2011 and 2015 a total of 1,685 patients in Georgia received treatment with pegylated interferon and ribavirin[12]; we do not include these treatments in the model. The elimination program was initiated on 28 April 2015, with treatment initially prioritized to patients with advanced liver disease[13]. Treatment is introduced in the model from May 2015 using monthly treatment numbers from the elimination program data, allocated by liver disease state (Supplementary Table 7). Liver disease was measured through transient elastography or by FIB-4[8,14], with cirrhosis defined as F4 or FIB-4 > 3.25.

From May 2015 to March 2016, sofosbuvir and ribavirin were used to initiate 7,097 patients on treatment, achieving per-protocol sustained virologic response (SVR) of 80.4%. From April 2016 to February 2019, sofosbuvir/ledipasvir was used to initiate 47,216 patients, with a per-protocol SVR of 98.3% (Supplementary Table 7). The latter SVR rate is used for projected treatments.

The treatment parameter $\sigma_k^i(t)$ is calculated from May 2015 to February 2019 according to the monthly number of treatments initiated in each liver disease state (mild/none, moderate, cirrhosis, decompensated cirrhosis; Supplementary Table 7). At each time point in the model, for each liver disease category the monthly treatment number is converted to an annual treatment number and divided by the number of individuals in all of the corresponding infected liver disease states (regardless of PWID status, age, or gender) to get the proportion of individuals to treat, which is assumed to be 0 if there are no eligible individuals. These proportions are then multiplied by the number of individuals in each infected compartment to calculate the annual number of treatments that are initiated at that time point. From March 2019 onwards, at each time point the annual number of treatments is allocated proportionally across all infected individuals with eligible liver disease states (ie excluding hepatocellular carcinoma) regardless of PWID status, age, or gender.

In the sensitivity analysis, alternative strategies for the distribution of treatment were explored, in which PWID were excluded from treatment or targeted for treatment, or 80% of patients with compensated cirrhosis are treated in each year. When PWID are excluded from treatment the number of treatments eligible for treatment excluded those in the current PWID category, such that the same number of treatments are distributed among a smaller population of infected individuals. When PWID are targeted for treatment the proportion of PWID treated is calculated to be double the proportion of non-PWID treated, such that the same number of treatments are allocated. When patients with cirrhosis are targeted for treatment, initially 80% of patients with compensated cirrhosis are allocated treatments, and then the remaining number of treatments are allocated proportionally across all remaining eligible categories.

For each scenario, the number of treatments required to reach a 90% reduction in adult hepatitis C prevalence from 2015 to the end of 2020 was fitted for each parameter set using the Matlab function lsqnonlin. Model runs which failed to fit were excluded from further analysis; between 0 and 3 parameter sets failed to fit in each scenario evaluated.

Adjusted SVR

In the baseline model, we use an adjusted SVR rate for pre-cirrhotic and cirrhotic treated patients. These rates assumed the per-protocol SVR rate for all individuals that achieved the end of treatment (78% of treatment initiates) and assumed a reduced SVR rate based on studies of shorter treatment regimens for those individuals that did not achieve the end of treatment due to being lost to follow up during treatment[15]. The reduced SVR rate for those lost to follow up was calculated by fitting a logarithmic trend line to mean SVR by treatment durations of 4, 6, 8, and 12 weeks[15–17] (Supplementary Figure 3), and integrating this function to determine the area under the curve of 6.6 cure-weeks. Assuming that patients are equally likely to be lost to follow up at any time point of treatment, we calculated the average cure rate over 12 weeks of treatment as 0.55.

Model Calibration

A version of Markov Chain Monte Carlo Approximate Bayesian Computation (MCMC-ABC) was used to fit the model by constraining prior ranges of model parameters based on fit to summary statistics from the calibration data (Supplementary Table 6). We used the package EasyABC in R[18,19] with the Wegmann method[20], which uses a partial least-squares transformation to weight the summary statistics to reduce the computation time needed to approximate the posterior. The model was initialized with 30,000 calibration steps and the best 0.5% of calibration simulations used to set the tolerance level. The chain was then run until 70,000 parameter sets were accepted using 1 standard deviation as the width for the proposal range of new parameter values at each step, and with 1 step between samples. All prior distributions were uniform. Parameter sets accepted in the first phase were then filtered as described in the main text.

Hepatitis C Incidence in PWID

Unpublished data on incident HCV infections in Georgia were received from M. Aladashvili of the Infectious Diseases, AIDS, and Clinical Immunology Research Center in Tbilisi, Georgia. The studies in which the data were collected have been partially published[21,22].

Patients were recruited from the cities of Tbilisi, Batumi, and Poti, and patients were enrolled over time during two studies from 1997-1999 and 2000-2001. In the first study, 926 PWID were

recruited and evaluated with a baseline assessment and two follow ups at 6 month intervals. In the second study, 469 PWID who had participated in the first study were recruited again, and 114 new PWID were recruited, and included up to three evaluations at 6 month intervals as in the previous study. At each visit participants were tested for HIV and HCV antibodies if they had not already had a positive test at a previous visit.

Incidence was calculated for the period 1997-2001. There were 102 incident cases of hepatitis C in 423 individuals anti-HCV negative at baseline and followed up for 698 person years, resulting in an incidence rate of 14.6 (12.0 - 17.7) per 100 person years.

Supplementary Tables

Supplementary Table 1

Age-varying demographic parameter rates used in the model of Hepatitis C in Georgia. Death rates adapted from the WHO Global Health Observatory data repository life tables for the country of Georgia for 2010-2015 (http://apps.who.int/gho/data/view.main.60610?lang=en).

	Aging rate (years^{-1})	Baseline death rate	
Age group (years)	α	μ_{female}	μ_{male}
<15	0.067	0.0005	0.0005
15-17	0.333	0.0005	0.0010
18-24	0.143	0.0005	0.0010
25-29	0.2	0.0005	0.0010
30-34	0.2	0.0010	0.0020
35-39	0.2	0.0010	0.0020
40-44	0.2	0.0010	0.0040
45-49	0.2	0.0020	0.0070
50+	NA	0.0400	0.0700

*Aging rate is defined as the inverse duration spent in each age category

Supplementary Table 2

Parameters related to injecting drug use, fitted in the model of Hepatitis C in Georgia.

Symbol	Parameter description	Unit	Prior range	Source
τ_2	Year Injecting scales up	Year	1980-1995	Breakdown of Soviet Union; [23,24]
Δ	Length of heightened period of recruitment to injecting	time in years	1-30	-
ψ	Baseline initiation rate to injecting	annual rate	0.0001 - 0.1	-
f_ψ	Relative injecting recruitment rate for females	ratio	0 - 0.045	Proportion of female PWID in BBS[7,22,25] and proportion female of those reporting ever injecting in NS2015[26]
δ_1	Factor increase in injecting recruitment during heightened period	ratio of pre-peak value	2-10	-
δ_2	Factor decrease in injecting recruitment after heightened period	ratio of peak value	2-20	-
ϕ_1	Duration of injecting for age <29 PWID	time in years	5-50	-
ϕ_2	Duration of injecting for age 30-49 PWID	time in years	5-50	-

ϕ_3	Duration of injecting for age 50+ PWID	time in years	5-50	-
ν	Standardized mortality ratio for PWID	ratio	7.22 - 11.28	[27]
M	Assortative mixing between <30 vs 30+ PWID	ratio	0-1	-

*PWID: people who inject drugs; BBS: Biological and Behavioral Surveillance surveys; NS2015: national Hepatitis C prevalence survey conducted in Georgia in 2015

Supplementary Table 3

HCV transmission parameters fitted in the model of Hepatitis C in Georgia.

Symbol	Parameter description	Unit	Prior range	Source
β	General population HCV transmission	annual effective contact rate	0.001 - 0.2	-
ϵ	Reduction in β after year τ_3	ratio	0.01 - 0.5	-
τ_3	Year β changes	year	1994 - 2000	[2,3]
θ	PWID HCV transmission before intervention scale-up	annual effective contact rate	0.001 - 0.5	-

*PWID: people who inject drugs; HCV: hepatitis C virus

Supplementary Table 4

Harm reduction parameters fitted in the model of Hepatitis C in Georgia.

Symbol	Parameter description	Unit	Prior range	Source
ρ_o	Effectiveness of OST	ratio	0.4-0.63	[6] global estimate
ρ_n	Effectiveness of NSP [low intervention effect model]	ratio	0.09-0.62	[6] Europe estimate
ρ_{2002}	Reduction in PWID HCV transmission correlated with NSP from 2002 [high intervention effect model]	ratio	0-1	-
ρ_{2012}	Reduction in PWID HCV transmission correlated with NSP scale up after 10 years (2012) [high intervention effect model]	ratio	0-1	-

*PWID: people who inject drugs; OST: opioid substitution therapy; NSP: needle and syringe provision; HCV: hepatitis C virus;

Supplementary Table 5

Liver disease progression parameters fitted in the model of Hepatitis C in Georgia.

Symbol	Parameter description	Unit	Prior range	Source
γ_1	Progression mild to moderate fibrosis	annual transition probability	0.018 - 0.033	[9]
γ_2	Progression moderate fibrosis to compensated cirrhosis	annual transition probability	0.025 - 0.052	[9]
χ_1	Progression compensated cirrhosis to decompensated cirrhosis	annual transition probability	0.022 - 0.0461	[9]
χ_{HR1}	Hazard ratio of progression to DC after SVR	ratio	0.03 - 0.20	[10]
χ_2	Progression compensated cirrhosis or decompensated cirrhosis to HCC	annual transition probability	0.0016 - 0.039	[9]
χ_{HR2}	Hazard ratio of progression to HCC after SVR	ratio	0.16 - 0.35	[11]

ζ_1	Progression decompensated cirrhosis to death	annual transition probability	0.11 - 0.15	[9]
ζ_2	Progression HCC to death	annual transition probability	0.37 - 0.49	[9]

*DC: decompensated cirrhosis; SVR: sustained virologic response; HCC: hepatocellular carcinoma

Supplementary Table 6

Summary statistics used to fit model of Hepatitis C in Georgia. Antibody prevalence from PWID serosurveys was converted to chronic prevalence by using multiplicative factor of 72% based on chronic prevalence among HCV antibody positive in 2015 general population serosurvey.

Statistic	Year	Target value	Source
Population size	2015	3.72 million	[28]
Population of PWID	2014	49.7 thousand	[1]
Proportion PWID age 30-49	1998	0.368	[22]
Proportion PWID age 18-29	1998	0.632	[22]
Proportion PWID age 30-49	2015	0.603	[25]
Proportion PWID age 18-29	2015	0.194	[25]
Percentage of PWID that are female	2015	2.00%	[25]
PWID hepatitis C prevalence	2015	51%	[25]
PWID hepatitis C prevalence age 18-24 years	2015	15.50%	[25]
PWID hepatitis C prevalence age 25+ years	2015	53.70%	[25]
Ratio of PWID hepatitis C prevalence 2006/PWID hepatitis C prevalence 2015	NA	0.86	[7,25]
Ratio of hepatitis C prevalence in PWID <30 years 2015 / 1997 [high intervention effect model only]	NA	0.5	[22,25]
Overall hepatitis C prevalence age ≥ 18 years	2015	5.40%	[26]
Hepatitis C prevalence age 18-29 years	2015	1.40%	[26]
Hepatitis C prevalence age 30-49 years	2015	8.80%	[26]
Overall hepatitis C prevalence age 50+ years	2015	4.20%	[26]
Female hepatitis C prevalence age ≥ 18 years	2015	2.20%	[26]
Female hepatitis C prevalence age 18-29 years	2015	0.80%	[26]
Female hepatitis C prevalence age 30-49 years	2015	2.10%	[26]
Female hepatitis C prevalence age 50+ years	2015	2.80%	[26]
Overall Male hepatitis C prevalence age ≥ 18 years	2015	9.00%	[26]
Male hepatitis C prevalence age 18-29 years	2015	1.90%	[26]
Male hepatitis C prevalence age 30-49 years	2015	15.70%	[26]
Male hepatitis C prevalence age 50+ years	2015	6.00%	[26]
Ratio male hepatitis C prevalence age 30-49 to age 50+ years	2015	2.6	[26]

*PWID: people who inject drugs; HCV: hepatitis C virus

Supplementary Table 7

Treatments initiated during the Hepatitis C elimination program in Georgia, by liver disease state

Month-Year	Liver disease state				Total
	None/mild	Moderate	Cirrhosis	Decompensated Cirrhosis	
May-15	1	56	237	5	298
Jun-15	1	119	436	5	562
Jul-15	9	318	669	4	1000
Aug-15	1	415	706	3	1125
Sep-15	1	138	147	1	287
Oct-15	6	528	600	2	1136
Nov-15	11	322	302	2	637
Dec-15	20	479	392	0	891
Jan-16	0	6	8	0	15
Feb-16	18	350	260	0	628
Mar-16	8	274	235	1	518
Apr-16	25	753	568	0	1346
May-16	22	463	327	0	811
Jun-16	16	753	394	0	1164
Jul-16	467	591	199	6	1263
Aug-16	1802	1273	209	12	3296
Sep-16	2479	1784	301	30	4594
Oct-16	1986	1436	249	20	3691
Nov-16	1101	893	170	24	2188
Dec-16	1070	846	202	22	2140
Jan-17	945	810	189	21	1965
Feb-17	677	622	128	32	1460
Mar-17	611	594	157	20	1382
Apr-17	598	525	122	17	1262
May-17	622	564	147	21	1354
Jun-17	527	496	118	21	1162
Jul-17	555	479	115	15	1164
Aug-17	473	406	108	16	1004
Sep-17	485	434	104	18	1041
Oct-17	485	399	119	20	1023
Nov-17	501	426	119	20	1065
Dec-17	418	369	105	15	908
Jan-18	166	141	33	2	342
Feb-18	495	408	111	13	1027
Mar-18	745	649	164	29	1586
Apr-18	54	49	17	1	121
May-18	405	404	125	26	959
Jun-18	434	420	100	21	975
Jul-18	337	298	79	14	729
Aug-18	319	355	88	20	782
Sep-18	551	403	109	22	1085
Oct-18	548	384	117	28	1078
Nov-18	408	290	88	21	807
Dec-18	376	255	68	17	716
Jan-19	416	286	80	19	801
Feb-19	482	333	93	17	925

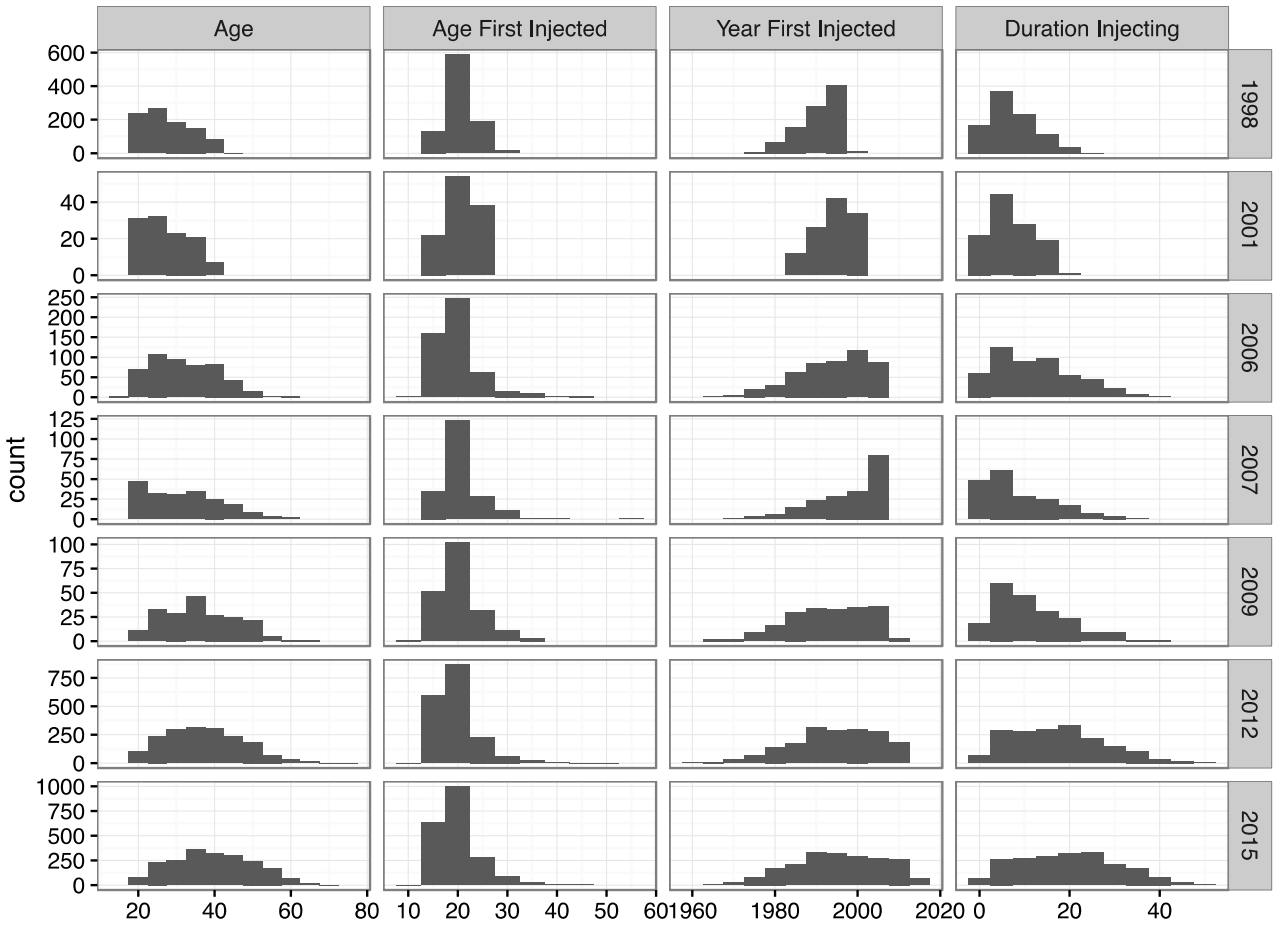
Supplementary Table 8

Proportion of variation in number of treatments required to reach elimination explained by uncertainty in different parameters in the baseline treatment scale up scenario; only parameters with proportion greater than 0.5% are included.

Symbol	Parameter description	% explained variance
B	Annual birth rate	35.9
Δ	Length of heightened period	16.8
δ_1	Factor increase in injecting recruitment during heightened period	13.9
ψ	Baseline initiation rate to injecting	10.5
τ_2	Year Injecting scales up	7.8
ϵ	Reduction in β	3.9
ϕ_2	Duration of injecting for age 30-49 PWID	1.7
δ_2	Factor decrease in injecting recruitment after heightened period	1.7
f_ψ	Relative injecting recruitment rate for females	1.6
ν	Standardized mortality ratio for PWID	1.3
ζ_2	Progression HCC to death	1.3
β	General population transmission	0.9
γ_2	Progression moderate fibrosis to compensated cirrhosis	0.7
ρ_{2002}	Reduction in PWID HCV transmission correlated with NSP from 2002	0.7
ϕ_1	Duration of injecting for age <29 PWID	0.6

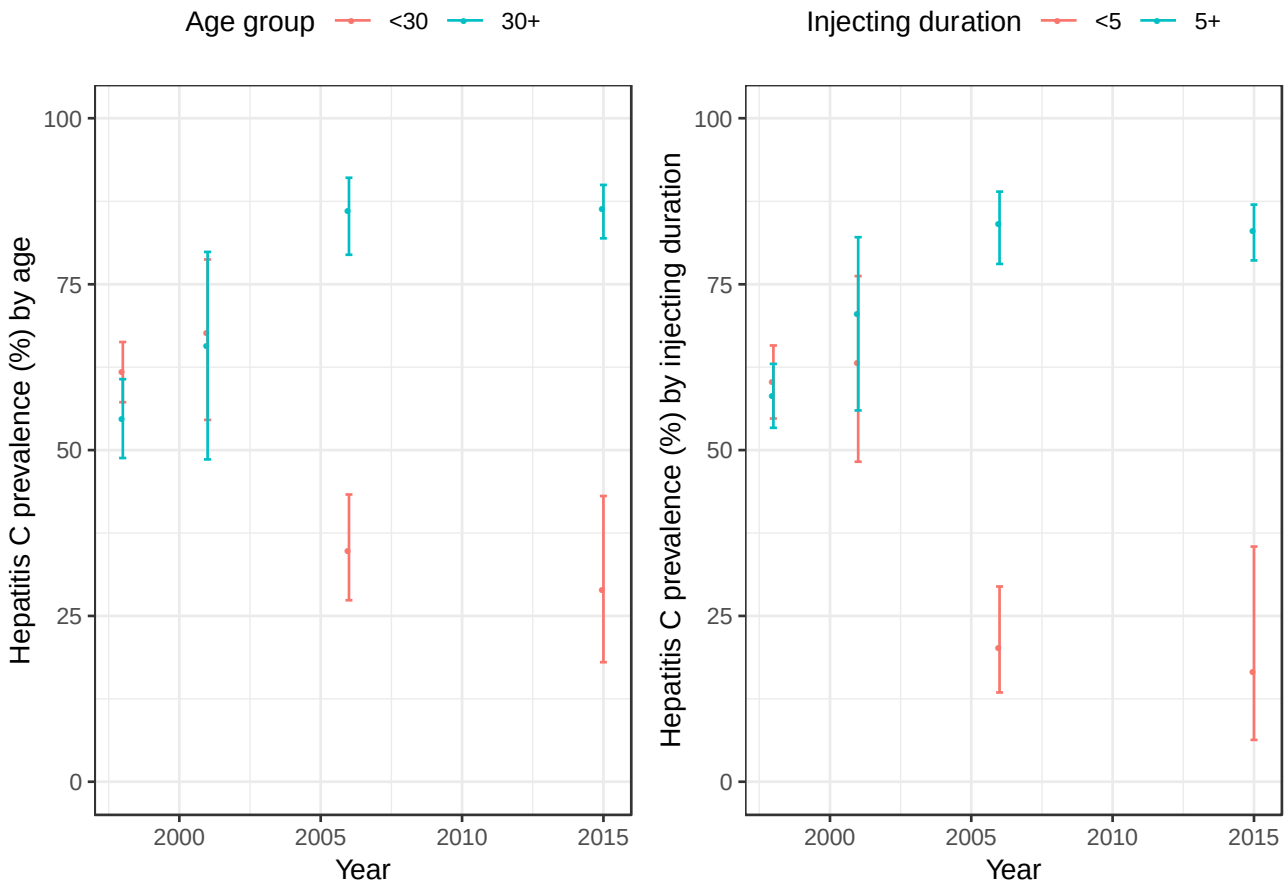
*PWID: people who inject drugs; HCV: hepatitis C virus; NSP: needle and syringe provision; HCC: hepatocellular carcinoma

Supplementary Figures



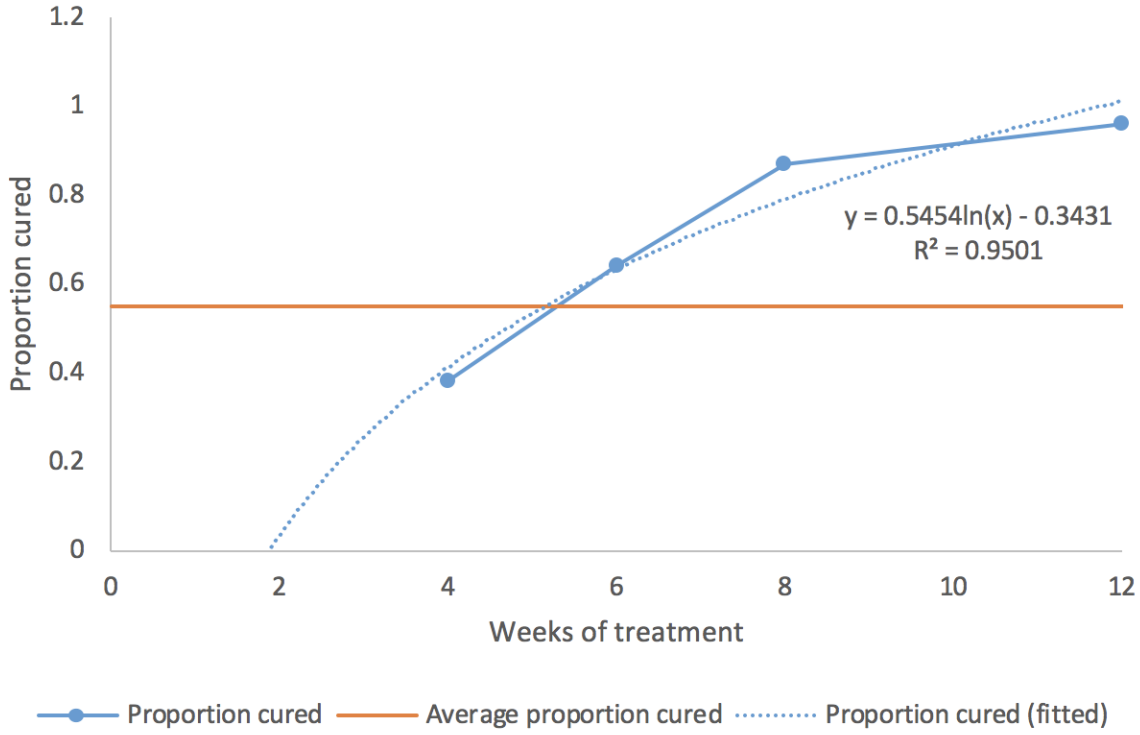
Supplementary Figure 1

Histograms of demographics of people who inject drugs in Georgia compiled from behavioral surveys and Integrated Biological and Behavioral Surveillance surveys[4,5,21,22,25,29], showing current age distribution at time of each survey, reported age at first injection, year first injected, and calculated duration injecting.



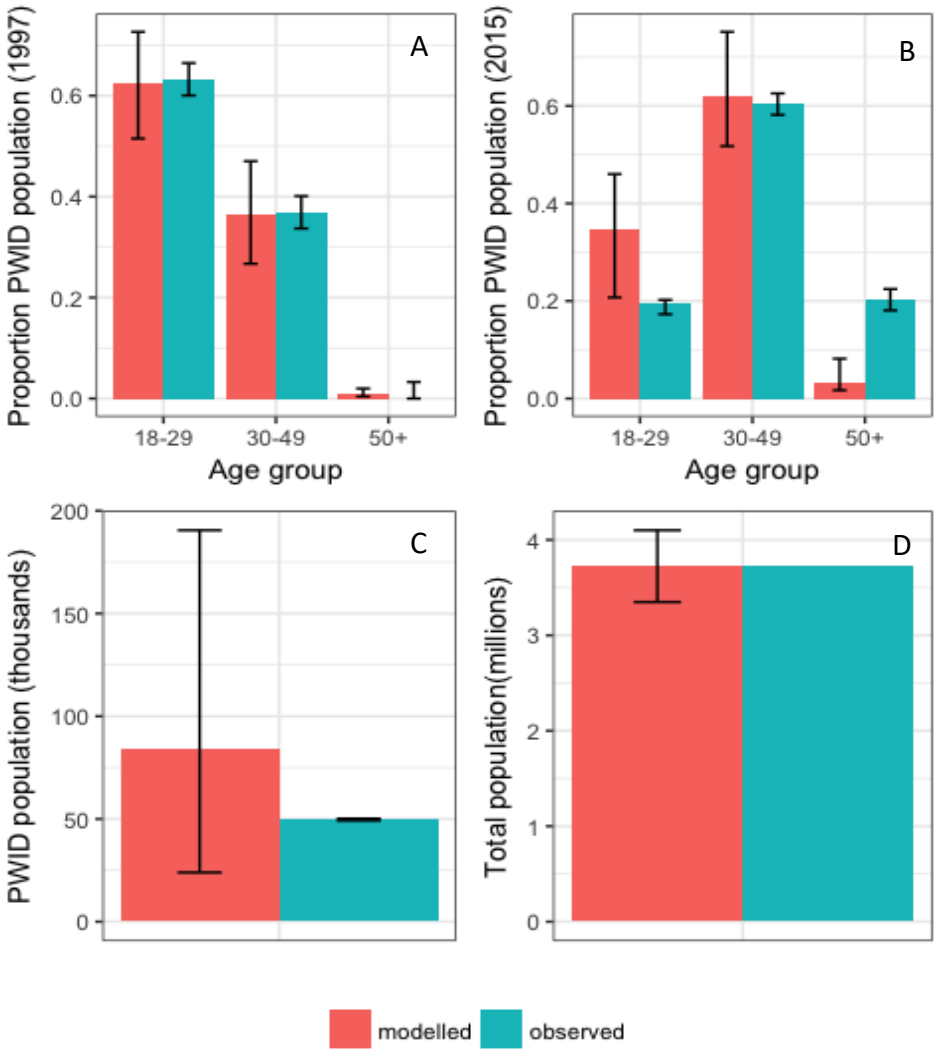
Supplementary Figure 2

Hepatitis C prevalence (mean and 95% confidence intervals) in people who inject drugs in Tbilisi, Georgia over time[4,5,21,22,25,29], grouped by age (left plot; < 30 years versus ≥30 years old) or duration of injecting (right plot; <5 years versus ≥5 years injecting drug use).



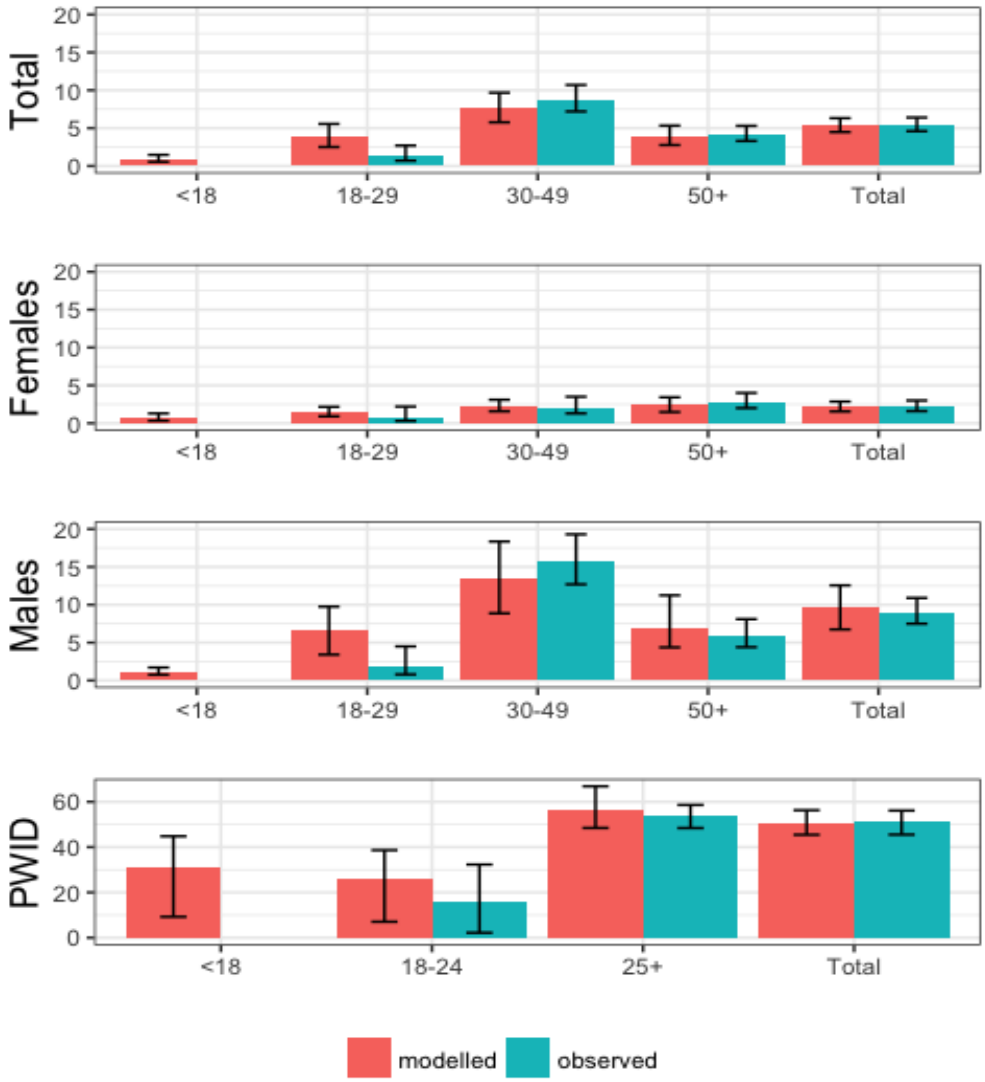
Supplementary Figure 3

Sustained virologic response rate achieved for different durations of treatment as used to estimate the average proportion cured of those lost to follow up, incorporating data for SVR by treatment durations of 4, 6, 8, and 12 weeks[15–17].



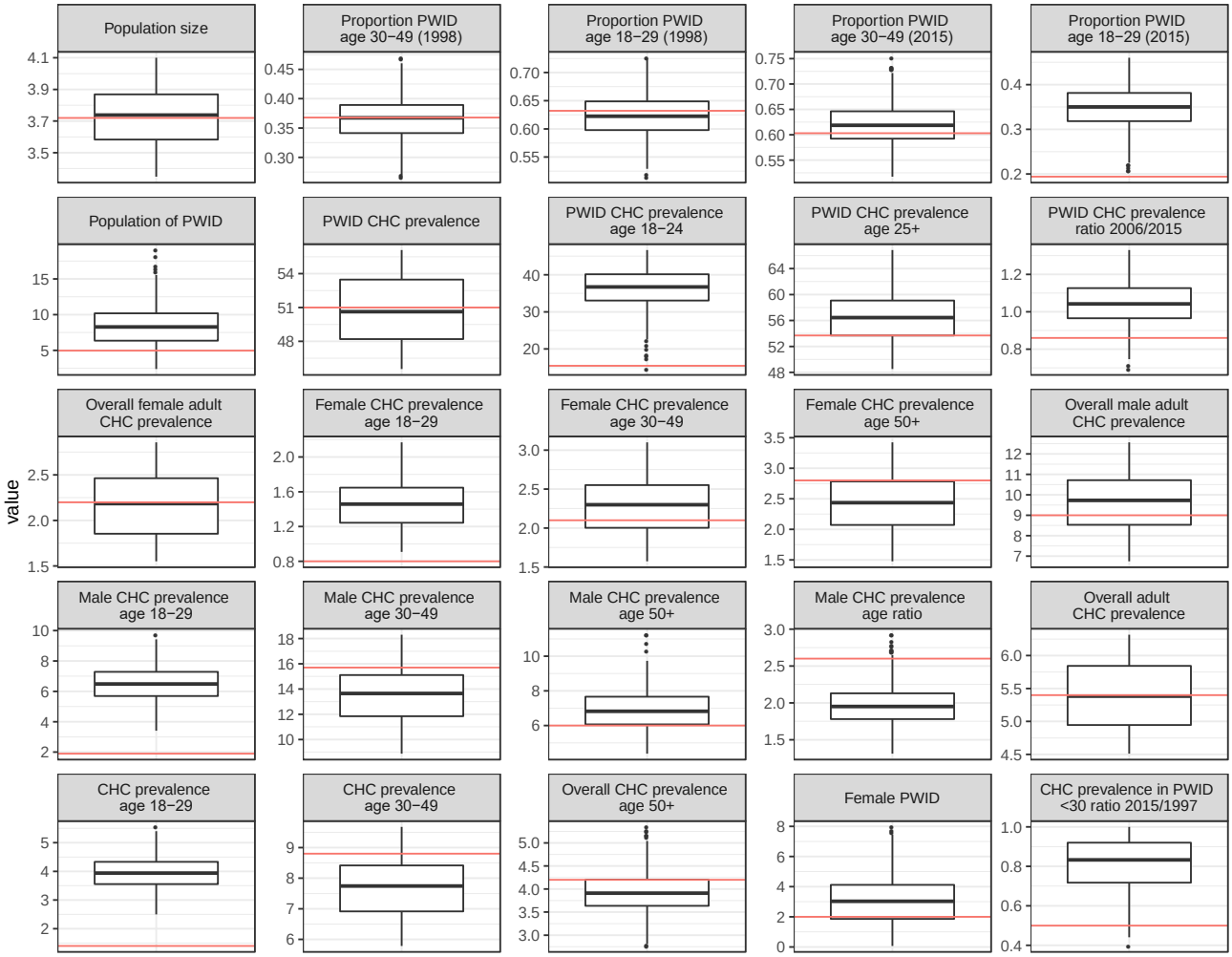
Supplementary Figure 4

Model fits to people who inject drugs (PWID) age distributions in 1997 (A) and 2015 (B), and to PWID population size (C) and general population size in Georgia (D). Bars are means and error bars show 95% confidence intervals for observed data and range for modelled parameter sets.



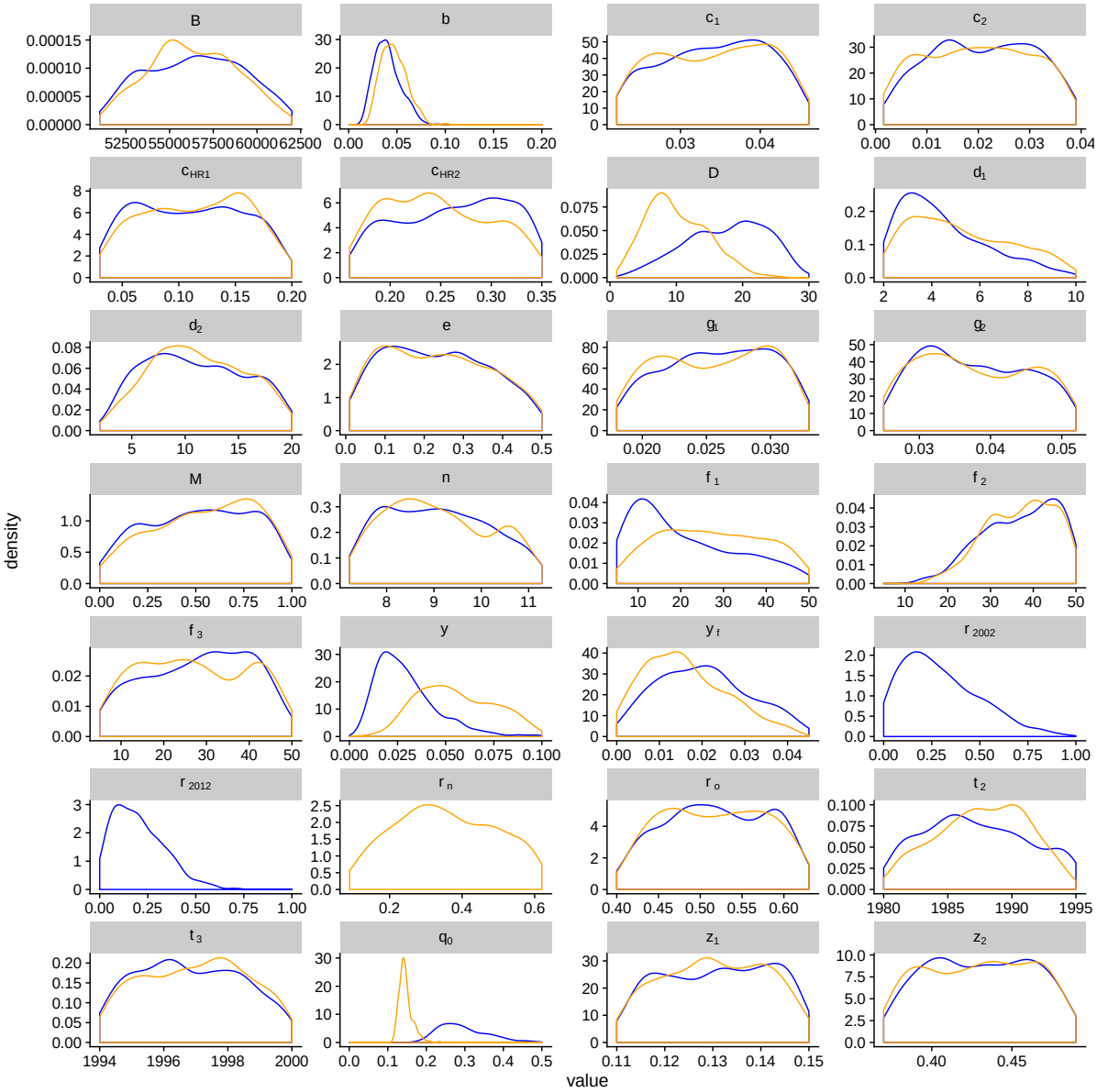
Supplementary Figure 5

Fits to percent chronic Hepatitis C infection by age and demographic group in 2015, total is total adult population (≥ 18). Total, male, and female observed data from national serosurvey, people who inject drugs (PWID) observed data from[22]. Bars are means and error bars show 95% confidence intervals for observed data and range for modelled parameter sets. No survey data are available for prevalence in individuals <18 years old.



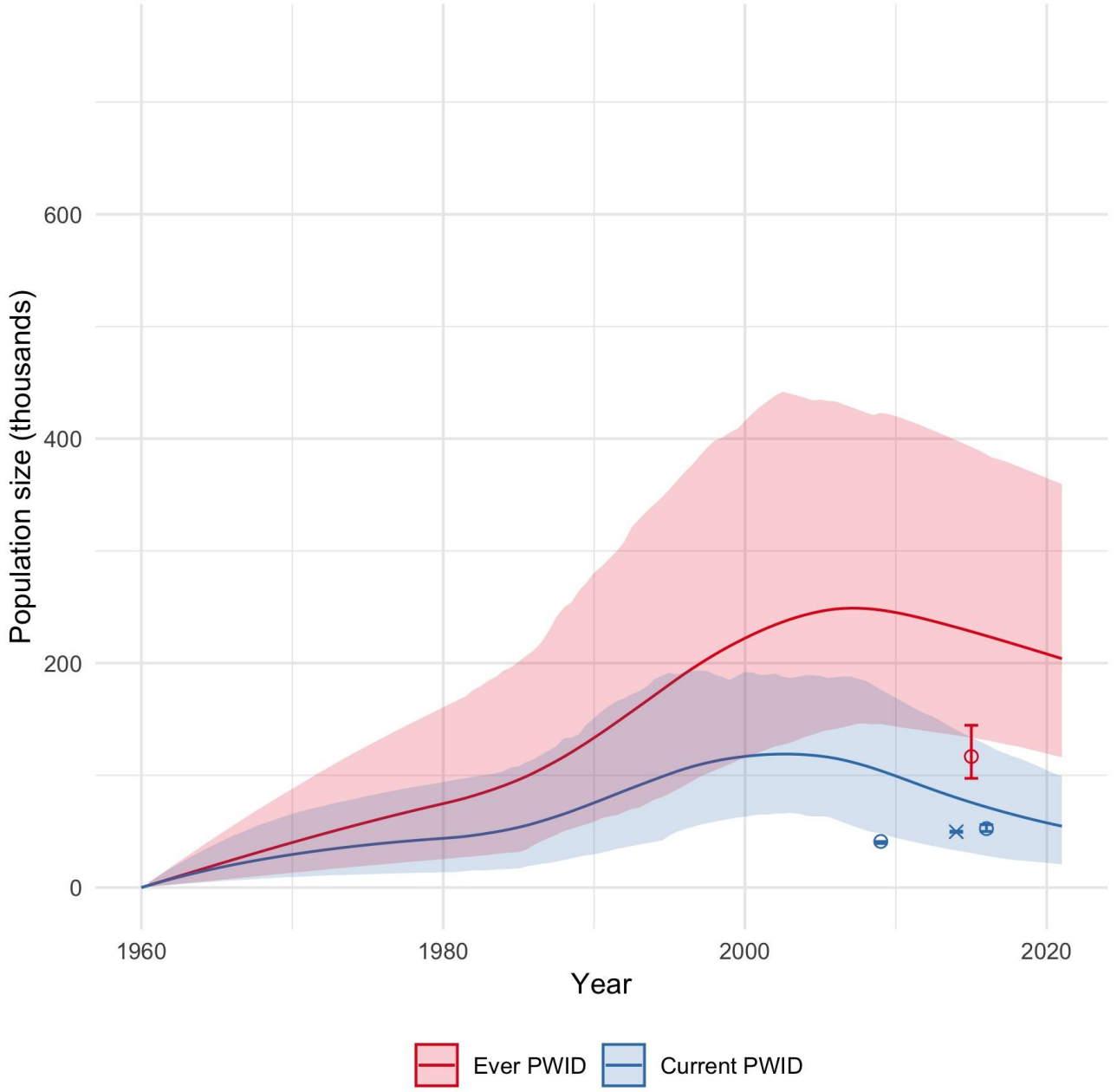
Supplementary Figure 6

Distribution of model fits (box plots) to target summary statistics (red lines) for baseline model fits. PWID: people who inject drugs; CHC: chronic Hepatitis C.



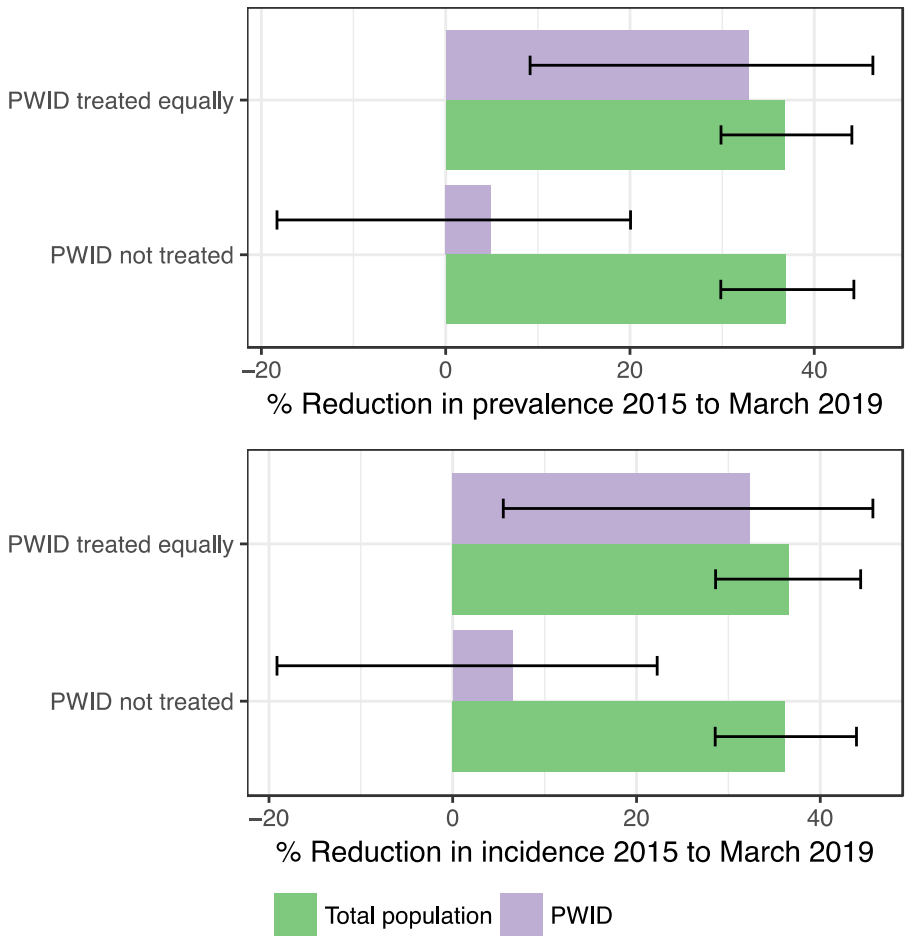
Supplementary Figure 7

Density plots of posterior distributions for alternative modelled structures, with blue showing baseline model fits and yellow showing sensitivity analysis Cochrane needle and syringe provision (NSP) analysis scenario. The range of the uniform prior distribution is shown as the extent of the x-axis.



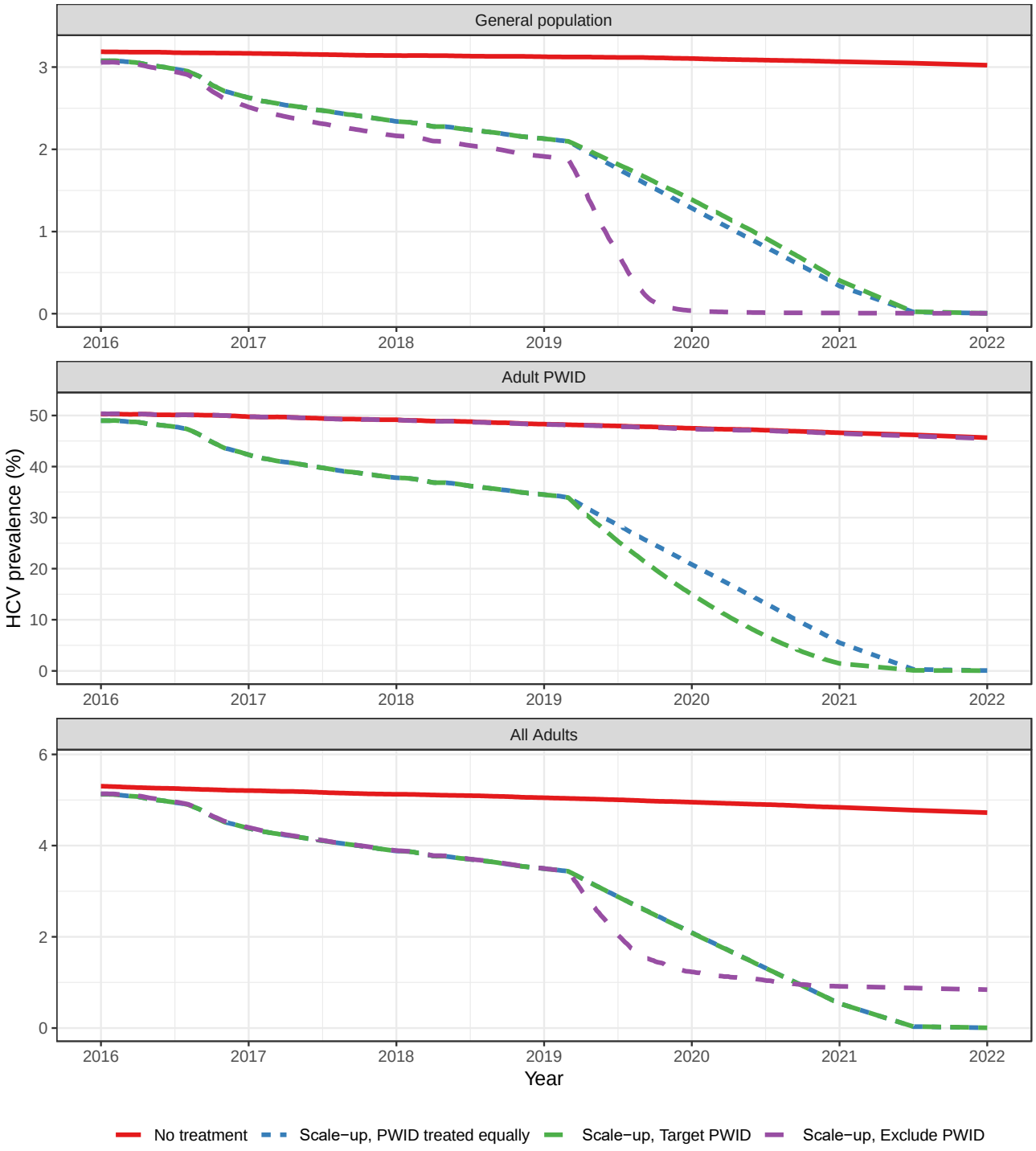
Supplementary Figure 8

Projected (mean and 95% credible interval) population size of current and ever people who inject drugs (PWID) (adults only) over time. Circles and crosses show available data of national population size estimates for ever PWID in 2015[26] and current PWID in 2009[30], 2014[1], 2016[31], with cross indicating data point (current PWID 2014) used for fitting.



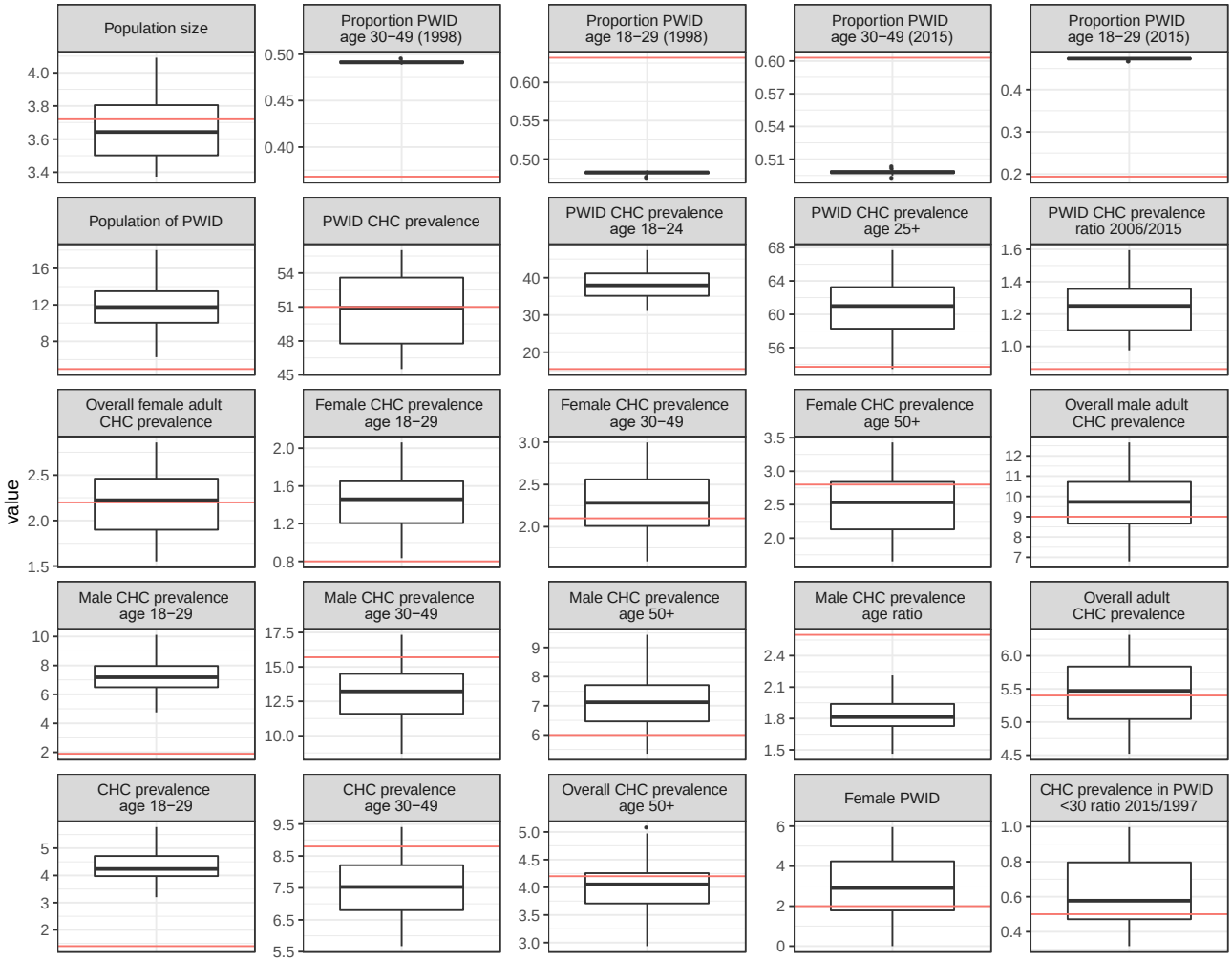
Supplementary Figure 9

Impact (percent reduction in Hepatitis C prevalence and incidence, and 95% credible intervals) achieved by March 2019 for the baseline intervention scenario with existing treatments when people who inject drugs (PWID) are included or excluded from treatment.



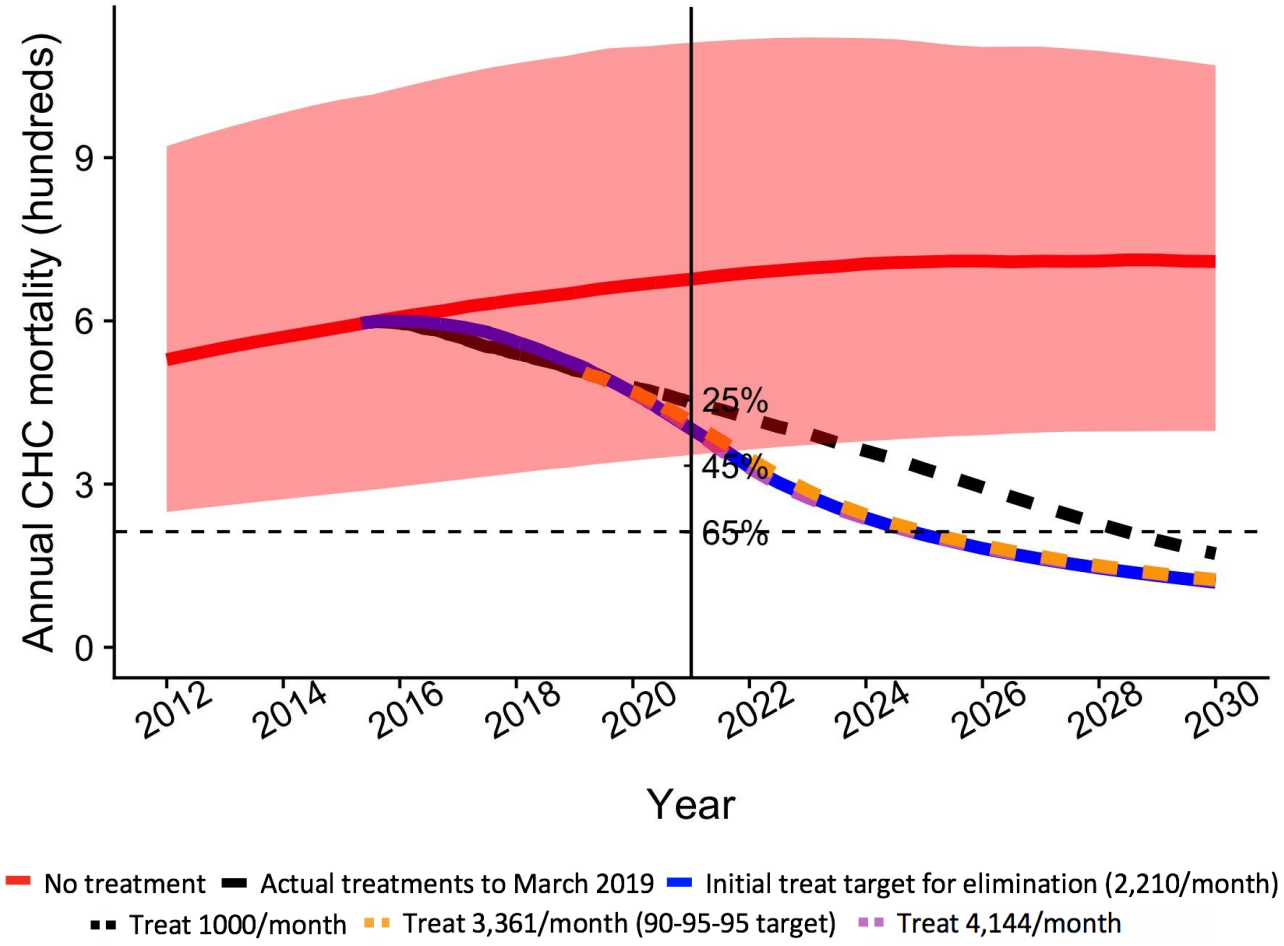
Supplementary Figure 10

HCV prevalence over time for general population (top), PWID (middle) and all adults (bottom) under alternative treatment scale-up scenarios where PWID are either treated equally (at the same rate as the general population), targeted (treated at twice the rate of the general population), or excluded from treatment, compared to no treatment. Lines show median prevalence from model runs fit to achieve a 90% reduction in total adult prevalence by end of 2020.



Supplementary Figure 11

Distribution of model fits (box plots) to target summary statistics (red lines) for parameter fitting scenario in which there is no peak in initiation of injecting drug use; A total of 156 parameter sets were accepted in this case. By comparison to the baseline model fits shown in Supplementary Figure 6, this approach does not achieve good fits to the age distributions of people who inject drugs (PWID) or differences in hepatitis C prevalence by age amongst PWID. PWID: people who inject drugs; CHC: chronic Hepatitis C.



Supplementary Figure 12

Model projected interim impact of annual hepatitis C mortality rate over time, to end of February 2019 and future impact of different treatment scenarios going forward to 2030 (note x-axis tick marks show beginning of labelled year). Vertical line shows target date of end of 2020, with the % reduction at end of 2020 compared to 2015, and horizontal dashed line shows the WHO target for mortality (65% decrease). Lines show median model projections: Solid red line, no treatment, with CrI (red shading); solid black line, actual treatments to February 2019; dashed black line, continuing 1000 treatments/month from March 2019; dashed yellow line, scale up to 3,361/month from March 2019 (90-95-95 target); dashed purple line, scale up to 4,144/month from March 2019; solid blue line, initial treatment target for elimination (2,210/month from 2015).

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